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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,828	CREECH ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,18 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/28/2005 has been entered.

Status of Application, Amendments, and/or Claims

2. The Amendment filed 07 November 2005 and the Declaration filed under 37 C.F.R. § 1.132 (filed 07 November 2005) have been received and entered in full. Claims 1-4, 6-7, and 18-19 are pending and are the subject of this Office Action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Drawings

4. The objection to the drawings as set forth at pg 3 of the previous Office Action (mailed 04 May 2005) is with withdrawn in view of Applicant's persuasive arguments (filed 07 November 2005).

Claim Rejections

4. The rejection of claims 1-4, 6-7, and 18-19 under 35 U.S.C. §101 and 35 U.S.C. § 112, first paragraph as set forth at pages 3-8 of the previous Office Action (mailed 04 May 2005) is withdrawn in view of Applicant's persuasive arguments (filed 07 November 2005). Additionally, the declaration under 37 CFR 1.132 filed 07 November 2005 has been considered and is sufficient to overcome the rejection of claims 1-4, 6-7, and 18-19 under 35 U.S.C. §101 and 35 U.S.C. § 112, first paragraph.

5. The rejections of claim 7 under 35 U.S.C. § 112, first paragraph (scope of enablement and written description) as set forth at pg 8-14 of the previous Office Action (04 May 2005) are withdrawn in view of Applicants persuasive arguments (filed 07 November 2005).

Maintained and/or New Rejections

Claim Rejections - 35 USC § 112, 1st Paragraph (scope of enablement)

6. Claims 1-4, 6, and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) an isolated nucleic acid that encodes a polypeptide comprising *the* amino acid sequence of SEQ ID NO:1; (2) an isolated nucleic acid comprising *the* nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3; and (3) an isolated nucleic acid encoding a cyclic nucleotide-gated cation channel subunit 3B (CNG3B) polypeptide, wherein the polypeptide comprises *the* amino acid sequence of SEQ ID NO:1 or comprises an amino acid sequence that shares 95% amino acid sequence identity to *the* amino acid sequence of SEQ ID NO:1; and wherein the polypeptide forms, with at least one cyclic nucleotide-gated channel

(CNG) alpha subunit, a cation channel having the characteristic of cyclic nucleotide-gating, does not reasonably provide enablement for (1) an isolated nucleic acid that encodes a polypeptide comprising *an* amino acid sequence of SEQ ID NO:1; (2) an isolated nucleic acid comprising *a* nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3; or (3) an isolated nucleic acid encoding a cyclic nucleotide-gated cation channel subunit 3B (CNG3B) polypeptide, wherein the polypeptide comprises an amino acid sequence that shares 85% or 90% amino acid sequence identity to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

7. The specification's disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

8. Claims 1 and 2 are drawn to a genus of nucleic acid molecules encoding a polypeptide comprising an amino acid sequence having at least 85% or 90% sequence identity to SEQ ID NO:1, claim 3 is drawn to a genus of nucleic acid molecules encoding a polypeptide comprising *an* amino acid sequence of SEQ ID NO:1, and claim 4 is drawn to a genus of nucleic acid molecules that comprise *a* nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3. However,

other than the protein of SEQ ID NO:1 and the DNA molecules of SEQ ID NO:2 and SEQ ID NO:3 that encode the protein, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 8-11 of the previous Office Action (mailed 04 May 2005). First, it is noted that the recitation "an amino acid sequence of SEQ ID NO:1" and "a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3" can be interpreted to mean a partial sequence consisting of as few as 2 amino acid residues or nucleotides, respectively. Thus, claims 3-4 are broadly interpreted by the Examiner as reading upon fragments of SEQ ID NOs: 1, 2, and 3, including sequences only 2 amino acids or nucleotides in length. However, the specification does not teach any variant, fragment, or derivative of the CNG3B proteins and polynucleotides other than the full-length amino acid sequences and the full-length nucleic acid sequences.

9. Applicants argue at pg 9 of the response (filed 07 November 2005) that cation channels of the CNG family are well studied and fully characterized in their structure, and that other beta subunits similar to CNG3B were known in the art at the time the instant application was filed. Based on this knowledge, the Applicant argue that a person of skill in the art would be able to easily perform a sequence comparison and determine conserved domains among CNG beta subunits, thus allowing an artisan to modify the amino acid residues not conserved among known CNG beta subunits while leaving those conserved residues unchanged in order to preserve functionality.

10. Applicant's arguments (filed 07 November 2005) as they pertain to the rejections have

been fully considered but are not found to be persuasive for the following reasons. It is noted that Applicant has not provided any evidence or reference of record to substantiate the allegation that cyclic nucleotide-gated (CNG) beta subunits have been characterized to the extent that one skilled in the art could readily determine, based on sequence information alone, which regions of the protein are tolerant to deletions or substitutions without altering the functionality of the molecule. It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

11. At page 10 of the response, Applicants argue that the instant case is factually distinct from the situations discussed by Wells and Ngo et al. (previous cited by Examiner). Applicants argue that, unlike the situations discussed in the references, in which protein functions are often inaccurately assigned based on the mere presence of a single domain with some level of sequence homology to a known functional domain in other proteins, there exists a closer and far more reliable correlation between the primary amino acid sequence of a CNG channel subunit and its biological function as a CNG cation channel subunit, and therefore argue that Wells and Ngo et al. does not support the Examiner's position.

12. Applicant's arguments have been fully considered but are not found to be persuasive. Ngo et al. and Wells et al. were cited by the Examiner to emphasize that positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Ngo et al. state that decades of research have failed to produce an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone (pg 492, 2nd full paragraph). Wells et al. teach that "it is possible to modulate protein function by mutation at many contact sites" and "to design large changes in function will often require mutation of more than one functional residue" (pg 8509, first paragraph; emphasis added). Wells et al. disclose that more pronounced deviations from simple additivity "can occur when the sites of mutations strongly interact with one another (by making direct contact or indirectly through electrostatic interactions or large structural perturbations) and/or when both sites function cooperatively" (pg 8515, column 2, 3rd full paragraph). For example, the stabilizing interaction between two side chains can be broken with one mutation and if the catalytic functions of two or more residues are interdependent, then a mutation of one residue can alter the functioning of the other(s) (pg 8512, column 2, 2nd full paragraph; pg 8515, column 1, 2nd full paragraph). Thus, while certain functional domains (e.g., the pore domain and the transmembrane domain) of CNG subunits have been identified, without more information the skilled artisan would not be able to determine, without undue experimentation, the structural conformation and function of CNG3B variants based upon linear amino acid sequences only. One skilled in the art would also not be able to determine, without undue experimentation, the positions in the CNG3B protein which are tolerant to change (e.g. such as by amino acid

substitutions or deletions), and the nature and extent of changes that can be made in these positions. The ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

13. Additionally, the Examiner has interpreted claim 19 as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The specification of the instant application teaches that the nucleic acid encoding the SNG3B polypeptide can be used in gene therapy (pg 53, line 5 through pg 58, line 3). However, there are no methods or working examples disclosed in the instant application whereby a CNG3B nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation since the specification has not taught any disease or condition for which gene therapy would be appropriate. (Please note that this issue could be overcome by amending claim 19 to recite, for example, "An isolated host cell...").

14. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen the same for activity, and to express a CNG3B nucleic acid in a cell of an organism for therapy; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity and how to introduce a CNG3B nucleic acid in the cell of an organism to be able

produce the encoded protein; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (written description)

15. Claims 1-4, 6, and 18-19 are also rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

16. The specification discloses two nucleotide sequences set forth as SEQ ID NO:2 and SEQ ID NO:3, which encode the polypeptide of SEQ ID NO:1. However, claims 1, 2, 3, and 4, as written, recite a genus of nucleic acid molecules that (1) encodes a polypeptide that comprises a subsequence having at least 85% amino acid sequence identity to SEQ ID NO:1; (2) encodes a polypeptide that comprises a subsequence having at least 90% amino acid sequence identity to SEQ ID NO:1; (3) encodes a polypeptide that comprises *an* amino acid sequence of SEQ ID NO:1; and (4) comprises *a* nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3. Thus, the claims are drawn to a large genus of DNA molecules which encompass a large number of nucleic acids that vary substantially, both in length and in nucleotide composition. As noted above, the recitation "an amino acid sequence of SEQ ID NO:1" and "a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3" can be interpreted to mean a partial sequence consisting of as few as 2

amino acid residues or nucleotides, respectively. Thus, claims 3-4 are broadly interpreted by the Examiner as reading upon fragments of SEQ ID NOs: 1, 2, and 3, including sequences only 2 amino acids or nucleotides in length. However, the specification does not teach any variant, fragment, or derivative of the CNG3B proteins and polynucleotides other than the full-length amino acid sequences and the full-length nucleic acid sequences.

17. Applicants argue at pg 11-12 of the response (filed 07 November 2005) that the claimed genus of nucleic acids is defined by their commonly shared functional features (e.g., encoding a polypeptide capable of forming, with at least another alpha subunit, a cyclic nucleotide gated cation channel) and structural features (encoding a polypeptide comprising a subsequence with at least 80% sequence identity to SEQ ID NO:1), and therefore meets the written description requirements. Applicants further argue that, given the CNG3B nucleotide coding sequence and the amino acid sequence of the CNG3B polypeptide, an ordinary skilled artisan would easily recognize which segments of the primary sequence correspond to the functional domains of the CNG beta subunit.

18. Applicant's arguments (filed 07 November 2005) as they pertain to the rejections have been fully considered but are not found to be persuasive for the following reasons. Specifically, Applicant has not described or shown possession of all nucleic acids that encode polypeptides 85% and 90% homologous to SEQ ID NO: 1, that still retain the function of SEQ ID NO: 1. Nor has Applicant described a representative number of species that have 85% and 90% homology to SEQ ID NO: 1, such that it is clear that they were in possession of a genus of nucleic acids that encode polypeptides functionally similar to SEQ ID NO: 1. Even one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed nucleic

acid molecules and polypeptides, and therefore, would not know how to make or use them. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factors present in the claims is a mere chemical property of the DNA in the form of a recitation of percent identity and the desired functional characteristic of "forming, with at least one alpha subunit, a cation channel having the characteristic of cyclic nucleotide-gating". There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function or that the described function is truly representative of all members of the claimed genus. Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus. It is noted that Applicant has not provided any evidence or reference of record to substantiate the allegation that given the CNG3B nucleotide coding sequence and the CNG3B polypeptide sequence, a skilled artisan would easily recognize which segments of the primary sequence correspond to the functional domains of the CNG beta subunit. It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important

evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

19. Applicant at pg 12-13 of the response disagrees with the Examiner's reading of *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 and application of *Fiddes* in the present case. Applicant argues that the fact pattern of *Fiddes* in not analogous to that of the present case. Applicant states that the patent applicants in *Fiddes* sought to patent a large genus of polypeptides and polynucleotides when they did not have in their possession any correct polynucleotide sequence. Applicant indicates that the Board's finding of inadequate written description was based on the notion that the claim of a genus of polynucleotides cannot be adequately supported when only an inaccurate polynucleotide sequence was disclosed. Applicant contends that in contrast to *Fiddes*, Applicant has in his possession both the amino acid sequence of the CNG3B subunit (SEQ ID NO:1) as well as the coding and complete nucleotide sequences that encode the CNG3B subunit (SEQ ID NOs: 2 and 3). Applicant also argues that the claims are not drawn to a broad genus of molecules without specific structural or functional definition. Applicant submits that both structural and functional features commonly shared by all members of the claimed genus have been described in detail.

20. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the fact pattern of *Fiddes* is analogous to that of the present case. In *Fiddes*, the claims directed to the broad class of mammalian FGF's did not have adequate written description since the patent only teaches the amino acid sequence for bovine pituitary FGF and the theoretical DNA sequence encoding that factor. Knowledge of the amino acid sequence of the

protein, along with the state of the art that establishes the degeneracy of the genetic code, does not establish the inventor's possession of the gene encoding the protein. In the instant application, the claims are drawn to a broad genus of nucleic acid molecules. The specification does not provide adequate written description for all nucleic acids that encode variants of SEQ ID NO:1 and wherein the polypeptide forms with at least one alpha subunit, a cation channel that has the characteristic of cyclic nucleotide-gating. In the instant application, a teaching of the coding nucleotide sequence (SEQ ID NO:2), the full-length nucleotide sequence (SEQ ID NO:3), and the amino acid sequence of the encoded protein (SEQ ID NO:1), is not sufficient to describe the distinguishing characteristics of the claimed genus. Accordingly, the specification does not provide adequate written description of the claimed genus.

21. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

22. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and DNA molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

23. Therefore, only the polynucleotide that encodes the CNG3B polypeptide of SEQ ID NO:1 and the DNA molecules of SEQ ID NO:2 and SEQ ID NO:3, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, 2nd Paragraph

24. Claims 1-7 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

25. Claim 1 is rejected as being indefinite because it is unclear whether the recitation of "alpha subunit" refers to a cyclic nucleotide-gated channel alpha subunit, or if it refers to an alpha subunit of any channel. Amending the claim to recite "one cyclic nucleotide-gated channel (CNG) alpha subunit", or the like, would be remedial.

26. Claims 1 and 2 are further indefinite for reciting "comprising a subsequence having at least...". Without knowing whether "a subsequence having at least X% amino acid sequence identity to SEQ ID NO:1" refers to a polypeptide that comprises a sequence that shares at least X% sequence identity to SEQ ID NO:1 or if it refers to a fragment of a polypeptide that shares at least X% sequence identity to SEQ ID NO:1 (it is noted that sequence identity is calculated

based on the shorter sequence), the metes and bounds of the claims cannot be determined.

27. Claim 3 is indefinite for reciting "an amino acid sequence of SEQ ID NO:1" in line 2 of the claim. Without knowing whether the indefinite article "an" is intended to mean "the amino acid sequence of SEQ ID NO:1" or any portion of the amino acid set forth as SEQ ID NO:1, the metes and bounds of the claim cannot be determined.

28. Claim 4 is indefinite for reciting "a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3" in line 2 of the claim. Without knowing whether the indefinite article "a" is intended to mean "the nucleotide acid sequence of SEQ ID NO:2 or SEQ ID NO:3" or any portion of the polynucleotide set forth as SEQ ID NO:2 or SEQ ID NO:3, the metes and bounds of the claim cannot be determined.

29. Claims 6-7 and 18-19 are rejected for depending from an indefinite claim.

Summary

30. No claim is allowed.

31. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kramer et al. (2001). Modulation of cyclic-nucleotide-gated channels and regulation of vertebrate phototransduction. The Journal of Experimental Biology. 204:2921-2931.

Peng et al. (2003). Achromatopsia-associated mutation in the human cone photoreceptor cyclic nucleotide-gated channel CNGB3 subunit alters the ligand sensitivity and pore properties of heteromeric channels. The Journal of Biological Chemistry. 278(36):34533-34540.

Broillet et al. (1999). Cyclic nucleotide-gated channels. Molecular mechanisms of activation. Annals New York Academy of Sciences. 868:730-40.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
March 29, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER